JUL 26 2007 By

IN THE CHAPTER STATES PATENT AND TRADEMARK OFFICE

Applicant:

Doron LANCET et al

Serial Number:

511,278/10

Filed:

October 22, 2004

For:

POLYMORPHIC OLFACTORY RECEPTOR GENES AND ARRAYS, KITS AND

METHODS UTILIZING INFORMATION DERIVED THEREFROM FOR

GENETIC TYPING OF INDIVIDUALS

Atty. Docket:

28364

Art Unit:

1634

Examiner:

Carla J. MYERS

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

DECLARATION OF DORON LANCET UNDER 37 CFR 1.132

I am presently employed Professor of Molecular Genetics at The Weizmann Institute of Science in Rehovot, Israel. I received my Ph.D. degree from Department of Chemical Immunology, The Weizmann Institute of Science, Rehovot, Israel. In 1978 and worked as a post-doctoral fellow at The Harvard University from 1978 to 1980 an. The Yale University School of Medicine from 1980 to 1981. Since completion of my postdoctoral work I have been employed at The Weizmann Institute of Science where I currently head the Crown Human Genome Center and am the Ralph and Lois Silver Professor of Human Genomics.

My research focuses on human molecular genetics, including the molecular genetics of olfactory receptors. Since the beginning of my career, I have published a number of scientific articles in highly regarded journals and books, and have presented my achievements at many international scientific conferences.

I am the inventor of the subject matter claimed in the above-referenced U.S. patent application.

I have read the Official action issued with respect to the above-identified application.

In this Official action, the Examiner has formulated the following rejections:

Claims 23-26, 28 and 29 are rejected under 35 USC § 101 as lacking utility;

Claims 23-26, 28 and 29 are rejected under 35 USC § 112, first paragraph, as lacking enablement and sufficient written description.

Appendix A enclosed herewith clearly demonstrates, while using the teachings of the instant application, that the C to T mutation at position 379 of OR11H7P (SEQ ID No.: 81) is linked to hypersomia to isovaleric acid both in an *in vivo* test of olfaction in human subjects and in an *in situ* assay of biological activity conducted in *Xenopus laevis* oocytes. These

28364

10/511,278
INVENTOR'S CURRICULUM VITAE

Name: Doron LANCET

Current Position: Head, Crown Human Genome Center

The Ralph and Lois Silver Professor of Human Genomics

Department of Molecular Genetics

The Weizmann Institute of Science, Rehovot 76100, Israel

Education

1967-1970 B.Sc. degree in Chemistry and Physics at the Hebrew University, Jerusalem, Israel, 1970.

1971-1972 Studies towards M.Sc. at the Feinberg Graduate School of the Weizmann Institute of Science,

Rehovot, Israel. Transferred directly to a Ph.D. program.

1973-1978 Studies and work towards Ph.D. at the Department of Chemical Immunology, The Weizmann

Institute of Science, Rehovot, Israel. Ph.D. degree in 1978.

Advisors: Dr. Israel Pecht and Dr. Michael Sela.

Title: "Kinetic and thermodynamic studies of hapten induced conformational changes in

immunoglobulins".

1978-1980 Post Doctoral training with Dr. Jack L. Strominger, Harvard University.

Subject: Structure, function and evolution of Human Histocompatibility Antigens (HLA).

1980-1981 Post Doctoral training with Dr. Gordon M. Shepherd, Yale University School of Medicine. Subject:

Activity mapping and neuronal modeling in the vertebrate olfactory pathway.

Recent Positions

1993-1997 Professor (tenured), the Department of Membrane Research and Biophysics, The Weizmann

Institute of Science, Rehovot. Subject: Molecular Biology, genetics and psychophysics of animal

and human chemoreception.

1995-1997 Head, Department of Membrane Research & Biophysics.

1997- Professor, Department of Molecular Genetics: Molecular Genomics and evolution of human

olfactory receptors, Genome analysis and bioinformatics, prebiotic evolution.

1997- Head, Crown Human Genome Center, The Weizmann Institute of Science.

Recent Academic Honors

| 1989-1990 | Eleanor Roosevelt Fellowship of the International Union against Cancer. |
|-----------|---|
| 1996 | Elected member, European Molecular Biology Organization (EMBO). |
| 1998 | The Frank Allison Linville's 1998 R.H. Wright Award in Olfactory Research |
| 2000- | Incumbent of the Ralph and Lois Silver Professor of Human Genomics |

Funding sources since 2000

| German-Israel Fu\oundation (GIF) | 1997-2000 |
|--|---------------------------------|
| Israel Ministry of Science (Natl.Lab. Genome Infrasructure) | 1997-2000, 2001-2003, 2004-2006 |
| Krupp Foundation | 1998-2002 |
| The Goldwasser Foundation | 2002-2005 |
| The Crown Human Genome Center | 1996-present |
| Xennex Inc. | 2003-present |
| U.S. National Institutes of Health (with Prof. Wyscoki, USA) | 2006-2009 |
| Tauber Foundation | 2005-2008 |
| Israel Science Foundation (with Prof. Lerer) | 2005-2008 |
| Israel-Korea collaboration | 2005-2007 |

Selected publications

Aloni, R., Olender, T. and Lancet, D. Ancient Genomic Architecture for Mammalian Olfactory Receptor Clusters. Genome Biol. (2006)1;7(10):R88[Epub ahead of print].

Menashe, I., Aloni, R. and Lancet, D. A probabilistic classifier for olfactory receptor pseudogenes. BMC Bioinformatics. 29;7:393 (2006).

Feldmesser, E., Olender, T., Khen, M., Yanai, I., Ophir, R. and Lancet, D. Widespread ectopic expression of olfactory receptors genes. BMC Genomics. 7:121 (2006).

Olender, T., Feldmesser, E., Atarot, T., Eisenstein, M. and Lancet, D. The olfactory receptor universe – from whole genome analysis to structure and evolution. Genet Mol Res. 3(4):545-53 (2004).

Olender, T., Fuchs, T., Linhart, C., Shamir, R., Adams, M., Kalush, F., Khen, M. and Lancet, D. The Canine Olfactory Subgenome. Genomics. 83:361-372 (2004).

Man, O., Gilad, Y. and Lancet, D. Prediction of the odorant binding site of olfactory receptor proteins by human-mouse comparisons. Protein Science 13:240-254 (2004).

Gilad, Y., Bustamante, C.D., Lancet, D. and Paabo, S. Natural selection on the olfactory receptor gene family in humans and chimpanzees. American Journal of Human Genetics. 73:489-501 (2003).

Menashe, I., Man, O., Lancet, D. and Gilad, Y. Different noses for different people. Nature Genetics. 34(2): 143-144 (2003).

Safran, M., Chalifa-Caspi, V., Shmueli, O., Olender, T., Lapidot, M., Rosen, N., Shmoish, M., Peter, Y., Glusman, G., Feldmesser, E., Adato, A., Peter, I., Khen, M., Atarot, T., Groner, Y. and Lancet, D. Human Gene-Centric Databases at the Weizmann Institute of Science: GeneCards, UDB, CroW 21 and HORDE. Nucleic Acids Research, 31(1):142-146 (2003).

Gilad, Y., Man, O., Paabo, S. and Lancet, D. Human specific loss of olfactory receptor genes. Proceedings of the National Academy of Sciences (PNAS) 100(6): 3324-3327 (2003).

Gilad, Y. and Lancet, D. Population differences in the human functional olfactory repertoire. Molecular Biology and Evolution, 20(3):307-314 (2003).

Menashe, I., Man, O., Lancet, D. and Gilad, Y. Population differences in haplotype structure within a human olfactory receptor gene cluster. Human Molecular Genetics, 11(12): 1381-1390 (2002).

Caticha, N., Palo Tejada, J.E., Lancet, D. and Domany, E. Computational Capacity of an Odorant Discrimator: the Linear Separability of Curves. Neural Computation. 14:2201-2220 (2002).

Rosenwald, S., Kafri, R. and Lancet, D. Test of a statistical model for molecular recognition in biological repertoires. Journal of Theoretical Biology, 216:327-336 (2002).

Carmel, L, Harel, D. and Lancet, D. Estimating the size of the olfactory repertoire. Bulleting of Mathematical Biology, 63:1063-1078 (2001).

Glusman, G., Yanai, I., Rubin, I. and Lancet, D. The complete human olfactory subgenome, Genome Research, 11:685-702 (2001).

Lapidot, M., Pilpel, Y., Gilad Y., Falcovitz, A., Haaf, T. and Lancet, D. Mouse-human Orthology relationships in an Olfactory Receptor Gene Cluster. Genomics, 71:296-306 (2001).

Fuchs, T., Glusman, G., Horn-Saban, S., Lancet, D. and Pilpel, Y. The Human Olfactory Subgenome: from sequence to structure and evolution. Human Genetics 108 (1):1-13 (2001).

Sharon, D., Gilad, Y., Glusman, G., Khen, M., Lancet, D. and Kalush, F. Identification and Characterization of Coding Single-nucleotide Polymorphisms within a Human Olfactory Receptor Gene Cluster. Gene, 260(1-2): 87-94 (2000).

Glusman, G., Bahar, A., Sharon, D., Pilpel, Y., White, J. and Lancet, D. The Olfactory receptor gene superfamily: data mining, classification and nomenclature. Mammalian Genome, 11:1016-1023 (2000).

Sosinsky, A., Glusman, G. and Lancet, D. The genomic structure of human olfactory receptor genes, Genomics, 70: 49-61 (2000).

Gilad, Y., Segre, D., Skorecki, K., Lancet, D. and Sharon, D. Dichotomy of single-nucleotide polymorphism haplotypes in olfactory receptor genes and pseudogenes. Nature Genetics, 26:221-224 (2000).

Glusman, G., Sosinsky, A., Ben-Asher, E., Avidan, N., Sonkin, D., Bahar, A., Rosenthal, A., Clifton, S., Roe, B., Ferraz, C., Demaille, J. and Lancet, D. Sequence, structure and evolution of a complete human olfactory receptor gene cluster. Genomics 63: 227-245 (2000).

Segre, D., Ben-Eli, D. and Lancet, D. Compositional genomes: prebiotic information transfer in mutually catalytic non-covalent assemblies. Proc. Natl. Acad. Sci (USA) 97 (8): 4112-4117 (2000).

Sharon, D., Glusman, G., Pilpel, Y., Khen, M., Gruetzmer, F., Haaf, T. and Lancet, D. Primate evolution of an olfactory receptor cluster: diversification by gene conversion and recent emergence of pseudogenes. Genomics 61:24-36 (1999).

Pilpel, Y. and Lancet D., The Variable and Conserved interfaces of modeled Olfactory Receptor Proteins. Protein Science 8: 969-977 (1999).

Buettner, J.A., Glusman, G., Ben-Arie, N., Ramos, P., Lancet, D. and Evans, G.A. Organization and Evolution of Olfactory Receptor Genes on Human Chromosome 11. Genomics 53: 56-68 (1998).

Glusman, G., Clifton, S., Roe, B. and Lancet, D. Sequence Analysis in the Olfactory Receptor Gene Cluster on Human Chromosome 17: Recombinatorial Events Affecting Receptor Diversity. Genomics 37(2): 147-160 (1996).

Singer, M.S., Weisinger-Lewin, Y., Lancet, D. and Shepherd, G.M. Positive Selection Moments Identify Potential Functional Residues in Human Olfactory Receptors. Receptors and Channels 4: 141-147 (1996).

Nekrasova, E., Sosinskaya, A., Natochin, M., Lancet, D. and Gat, U. Overexpression, Solubilization and Purification of Rat and Human Olfactory Receptor Proteins. European Journal of Biochemistry 238: 28-37 (1996).

Gat, U., Nekrasova, E., Lancet, D. and Natochin, M. Olfactory Receptor Proteins - Expression, Characterization and Partial Purification. Eur. J. Biochem. 225: 1157-1168 (1994).

Ben-Arie, N., Lancet, D., Taylor, C., Khen, M., Walker, N., Ledbetter, D.H., Carrozzo, R., Patel, K., Sheer, D., Lehrach, H. and North, M.A. Olfactory Receptor Gene Cluster on Human Chromosome 17: Possible Duplication of an Ancestral Receptor Repertoire. Human Mol. Genetics 3: 229-235 (1994).

Ben-Arie, N., Khen, M. and Lancet, D. Glutathione S-transferase in Rat Olfactory Epithelium: Purification, Molecular Properties and Odorant Biotransformation. D. Biochem. J. 292: 379-384 (1993).

Lancet, D., Sadovsky, E. and Seidemann, E. Probability Model for Molecular Recognition in Biological Receptor Repertoires: Significance to the Olfactory System. Proc. Natl. Acad. Sci., USA 90: 3715-3719 (1993).

Margalit, T. and Lancet, D. Expression of Olfactory Receptor and Transduction Genes during Rat Development. Developmental Brain Res. 73: 7-16 (1993).

Gross-Isseroff, R., Ophir, D., Bartana, A., Voet, H. and Lancet, D. Evidence for Genetic Determination in Human Twins of Olfactory Thresholds for a Standard Odorant. Neurosci. Lett. 141: 115-118 (1992).

Lazard, D., Zupko, K., Poria I., Nef, P., Lazarovits, J., Horn, S., Khen, M. and Lancet, D. Odorant Signal Termination by Olfactory UDP-Glucuronosyl Transferase. Nature 349: 790-793 (1991).

Zupko, K., Poria, Y. and Lancet, D. Immunolocalization of Cytochromes P-450olf1 and P-450olf2 in Rat Olfactory Mucosa Eur. J. Biochem. 196: 51-58 (1991).

Ludwig, J., Margalit, T., Eismann, E., Lancet, D. and Kaupp, B. Primary Structure of cAMP-Gated Channel from Bovine Olfactory Epithelium. FEBS lett. 270: 24-29 (1990).

Lazard, D., Tal, N., Rubinstein, M., Khen, M., Lancet, D. and Zupko, K. Biochemical and Immunochemical Analysis of Bovine Olfactory-Specific Cytochrome P-450IIA and UDP-Glucuronyl Transferase. Biochemistry 29: 7433-7440 (1990). Lazard, D., Barak, Y. and Lancet, D. Bovine olfactory Cilia Preparation: Thiol-Modulated Odorant-Sensitive Adenylyl Cyclase. Biochim. Biophys. Acta 1013: 68-72 (1989).

Roth, Y., Glickson, M., Neuman, R., Karni, A., Lancet, D., Gross-Iseroff, R., Ram, Z and Glovinsky, Y. Olfaction in Prolonged Administration of Pyridostigmine.J. Clin. Pharmacol. 29: 370-372 (1989).

Ophir, D. and Lancet, D. Expression of Intermediate Filaments and Desmoplakin in Vertebrate Olfactory Mucosa. The Anatomical Record 221: 754-760 (1988).

Gross-Isseroff, R. and Lancet, D. Concentration-Dependent Changes of Perceived Odor Quality. Chemical Senses 13: 191-204 (1988).

Gross-Isseroff, R., Stoler, M., Ophir, D., Lancet, D. and Sirota, P. Olfactory Sensitivity to Androstenone in Schizophrenic Patients. Biol. Psychiatry 22: 922-925 (1987).

Heldman, J. and Lancet, D. Cyclic AMP Dependent Protein Phosphorylation in Chemosensory Neurons: Identification of Cyclic Nucleotide Regulated Phosphoproteins in Olfactory Cilia. J. Neurochem. 47: 1527-1533 (1986).

Chen, Z., Pace, U., Heldman, J., Shapira, A. and Lancet, D. Isolated Frog Olfactory Cilia: a Preparation of Dendritic Membranes from Chemosensory Neurons. J. Neurosci. 6: 2146-2154 (1986).

Pace, U. and Lancet, D. Olfactory GTP-Binding Protein: Signal Transducing Polypeptide of Vertebrate Chemosensory Neurons. Proc. Natl. Acad. Sci. USA 83(13): 4947-4951 (1986).

Ophir, D., Gross-Isseroff, R., Lancet, D. and Marshak, G. Changes in Olfactory Acuity Induced by Total Inferior Turbinectomy. Arch. Otolaryngol. 122: 195-197 (1986).

Chen, Z., Pace, U., Ronen, D. and Lancet, D. Polypeptide gp95: A Unique Glycoprotein of Olfactory Cilia with Transmembrane Receptor Properties. J. Biol. Chem. 261: 1299-1305 (1986).

Chen, Z., Ophir, D. and Lancet, D. Monoclonal Antibodies to Glycoproteins of Frog Olfactory Cilia. Brain Research 368: 329-338 (1986).

Pace, U., Hanski, E., Salomon, Y. and Lancet, D. Odorant Sensitive Adenylate Cyclase May Mediate Olfactory Reception. Nature 316: 255-258 (1985).

Chen, Z. and Lancet, D. Membrane Proteins Unique to Vertebrate Olfactory Cilia: Candidates for Sensory Receptor Molecules. Proc. Natl. Acad. Sci. (PNAS) USA 81(6):1859-1863 (1984).

Lancet, D., Greer, C.A., Kauer, J.S. and Shepherd, G.M. Mapping of Odor-Related Neuronal activity in the Olfactory Bulb using High Resolution 2-Deoxyglucose Autoradiography. Proc. Natl. Acad. Sci. USA 79: 670-674 (1982).

Lancet, D., Kauer, J.S., Greer, C.A. and Shepherd, G.M. Localization of Odor-Related 2-deoxyglucose Uptake in the Olfactory Epithelium. Chemical Senses 6: 343-349 (1981).